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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/713,177	11/15/00	ERIKSON G	E1047/20048

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EXAMINER	
CHUNDURU, S	
ART UNIT	**PAPER NUMBER**
1656	5

DATE MAILED: 08/29/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/713,177	ERIKSON ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Arguments

1. Receipt of Amendment (Paper No.4) filed on July 9, 2001 is acknowledged.

2. Receipt of Applicant's response to office action (Paper No. 4) is acknowledged. Applicant's amendment and arguments filed in Paper No. 4 are fully considered but are deemed persuasive in part.

3. The following objection was in the previous office action:

The Disclosure is objected because of the following informalities:

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because the Oath / Declaration is not in permanent ink.

Applicants' amendment filed on July 9, 2001 obviated these objections. These objections are withdrawn in view of the amendment (Paper No. 4).

4. The following is the rejection under 35 U.S.C. 112 second paragraph:

Claims 41 and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because the claims 41 and 62 recite the terms 'homogeneous' and 'electrical circuit' which are vague and unclear because they does make the invention uncertain for not clearly point out what the terms mean to accomplish for.

Applicants' amendment filed on July 9, 2001 obviated this rejection. This rejection is withdrawn in view of the amendment (Paper No. 4).

5. The following is the rejection made under 35 U.S.C. 103(a) in the previous office action:

Claims 1-13, 15-17, 19-44, 47-58, 60, 62-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duck et al. (USPN. 5,660,988) and in view of Dervan et al. (USPN. 5,874,555).

Duck et al teach a method and composition for catalytic hybridization wherein they disclose that the hybridization cocktail comprises a target nucleic acid molecule with a probe containing a scissile linkage, and is complementary to the target nucleic acid and an excising agent (an enzyme) capable of cleaving the nucleic acid probe at the scissile linkage after formation of the target / probe hybrid (see column 2, line 19-37). They also disclose that (i) the nucleic acid probe could contain RNA, DNA and interspersed sequences as modified DNA or RNA (see column 8, 45-53); (ii) The target nucleic acid may be selected from diploid, polyploid organism or haploid cells (see column 2, lines 62-65); (iii) scissile linkage comprises from about 2 to about 100 nucleotides and the nucleic acid probe comprises from about 0 to 20 nucleotides or more (see column 8, lines 42-45); (iv) the excising enzyme is RNase H (see column 8, lines 54-62); the probe-target detection includes detectable markers such as fluorescent, chemiluminescent, ligand (biotin) and radiolabelled molecules (see column 9, lines 45-56); (v) the nucleic acid probe may be immobilized on a solid support (see column 9, lines 56-57); (vi) the probes could be chimeric and comprise base labile phosphoramidates such as N-base protected, cyanoethyl, or 2'-OH sugar protected phosphoramidates (see column 10, lines 49-62); a suitable tether may be covalently attached to the amino-modified oligonucleotide probe to

facilitate attachment to and function of the excising agent (see column 13, lines 15-21); the probe and target nucleic acid could be double-stranded or single stranded (see column 16, lines 50-67); the incubation temperature for the reaction is typically from about 60^0 c to about 70^0 C and the pH is 7.5 to 8.1 and the incubation time maybe from about 5 to 60 minutes or longer (see column 16, lines 24-38). However, they did not teach formation of multiplex structure and promoter of the probe.

Dervan et al. teach triplex structure formation by the method of hybridization of nucleic acid and oligonucleotide probes wherein they disclose that (i) the DNA may be obtained from genomic DNA (see column 6, lines 25-27) was hybridized with oligonucleotide probes equipped with DNA cleaving moiety (promoter) which includes oligonucleotide-EDTA-Fe, where EDTA is a chelator and Fe is a transition element having valency grater than one or chelator (EDTA) attached to intercalator methidium (see column 2, lines 43-52, column 1, lines 44-56 and column 10, lines 9-29); (ii) a portion of the triple helix structure is synthetic (see column 9, lines 28-35); (iii) the chelators or other cleavage moieties do not disrupt the hydrogen-base pair bonding (Watson-crick base pairing) between DNA or RNA sequences during triple helix formation (see column 10, lines 30-37); (iv) triplex formation could be analyzed by applying electrical force such as gel electrophoresis (see column 11, lines 19-26); (v) the oligonucleotide probe bind either in major or minor grove of the target nucleic acid depending on the symmetry of the cleavage pattern (see column 13, lines 13-26 and column 1, lines 44-56).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method of catalytic hybridization with triple helix formation to achieve expected advantage of identification of nucleic acid sequence or

variation in it. The motivation for this would have been an approach to detect formation of multiple helix structures in hybridization assays.

The rejection under USC 103(a) is maintained for the reasons of record stated below:

Applicants argue that combination of the teachings of Duck et al., Dervan et al. and does not disclose or suggest the claimed invention. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Duck et al. does teach the composition of catalytic hybridization comprising at least one probe nucleobase sequence, at least one scissile linkage and an enzyme that cleaves the said scissile linkage and suggested that the excising hybridized scissile linkage sequence is carried out with a double-stranded ribonuclease that excises ribonucleic acid sequences from a double-stranded DNA-RNA hybrid (see column 8, lines 54-62). The double-stranded DNA-RNA hybrid of the disclosure of Duck et al. indicates the multiplex structure claimed in the instant claim 1. The combination of the teachings of Duck et al. and Dervan et al. does motivate one skilled in the art to combine the teachings to generate a composition that comprises all the components nucleobase probe, scissile linkage and an enzyme in a hybridization medium with target nucleic acid. Though the teachings of Duck et al. suggest a catalytic hybridization composition, the teachings of Dervan et al. clearly points out the multiplex structure (a triplex formation) in the

hybridization method. Therefore, it is obvious that the above teachings do motivate a skilled artisan to arrive at the instant claimed invention.

Claims 14, 18, 45-46, 59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duck et al. (USPN. 5,660,988) and in view of Dervan et al. (USPN. 5,874,555) as applied to claims 1-13, 15-17, 19-44, 47-58, 60, 62-63 above, and further in view of Pinter et al. (USPN. 5,888,739) and Walder et al. (USPN. 5,403,711).

Duck et al. teach the catalytic hybridization comprising a nucleic acid probe with scissile linkage and an enzyme capable of cleaving the probe at scissile linkage after target-probe hybrid formation. Dervan et al. teach a triple helix formation during the target-probe hybridization. However, these references did not teach G-G quartet free multiplex structure, PCR amplified products as target nucleic acid, the probe to target ratio and the enzyme RNase H from E.coli.

Pinter et al. teach a method for the detection of nucleic acids using G-quartets wherein they disclose that G-quartets get disrupted in hybridization assays in the presence of complementary oligonucleotide probe sequence (see column 3, lines 55-67).

Walder et al. teach a method for catalytic hybridization amplification (CHA) wherein they disclose that (i) the cleavage reaction is catalyzed by the enzyme RNase H which is obtained from E.coli (see column 11, lines 9-29); (ii) the target nucleic acid can be obtained by polymerase chain reaction (see column 14, lines 65-68 and column 15, lines 1-14). They also disclose that the target to probe ratio as 1:100 to 1:1000 (see column 11, lines 50-62).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method of catalytic hybridization with triple helix formation, CHA and G-quartets formation to achieve expected advantage of identification

of nucleic acid sequence or variation in it based on the formation of multiplex structure. The motivation for this would have been an approach to detect formation of multiple helix structures in hybridization assays.

The rejection under USC 103(a) is withdrawn in view of the Applicants' arguments in Paper No. 4. This rejection is with drawn.

In the light of new prior art, new rejections are made in this office action:

Claim Rejections - 35 USC § 103

Claims 18, 24, 45, 49, 60-63 and the dependent claims are rejected under 35 U.S.C. 103(a) as being unpatentable over Duck et al. (USPN. 5,731,146) and in view of Walder et al. (USPN. 5, 403, 711).

Duck et al teach a method and composition for catalytic hybridization wherein they disclose that the hybridization cocktail comprises a target nucleic acid molecule with a probe containing a scissile linkage, and is complementary to the target nucleic acid and an excising agent (an enzyme) capable of cleaving the nucleic acid probe at the scissile linkage after formation of the target / probe hybrid (see column 2, line 19-37). They also disclose that (i) the nucleic acid probe could contain RNA, DNA and interspersed sequences as modified DNA or RNA (see column 8, 45-53); (ii) The target nucleic acid may be selected from diploid, polyploid organism or haploid cells (see column 2, lines 62-65); (iii) scissile linkage comprises from about 2 to about 100 nucleotides and the nucleic acid probe comprises from about 0 to 20 nucleotides or more (see column 8, lines 42-45); (iv) the excising enzyme is RNase H (see column 8, lines 54-62); the probe-target detection includes detectable markers such as fluorescent, chemiluminescent, ligand (biotin) and radiolabelled molecules (see column 9, lines 45-56); (v)

the nucleic acid probe may be immobilized on a solid support (see column 9, lines 56-57); (vi) the probes could be chimeric and comprise base labile phosphoramidates such as N-base protected, cyanoethyl, or 2'-OH sugar protected phosphoramidates (see column 10, lines 49-62); a suitable tether may be covalently attached to the amino-modified oligonucleotide probe to facilitate attachment to and function of the excising agent (see column 13, lines 15-21); the probe and target nucleic acid could be double-stranded or single stranded (see column 16, lines 50-67); the incubation temperature for the reaction is typically from about 60^0 c to about 70^0 C and the pH is 7.5 to 8.1 and the incubation time maybe from about 5 to 60 minutes or longer (see column 16, lines 24-38). However, they did not teach formation of multiplex structure.

Walder et al. teach a catalytic hybridization method wherein Walder discloses that the method includes (i) DNA synthesized from polymerase chain reaction (see column 14, lines 65-67 and column 15, lines 1-20); (ii) formation of probe- target duplexes and target to probe ratio being 1:100 to 1: 1000 (see column 7, lines 32-450 and column 11, lines 50-60); (iii) the cleavage enzyme used was RNase H from E.Coli (see column 11, lines 9-29); and the detection of extent of cleavage of the probe was determined using separation methods such as electrophoresis (electrical circuit).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method of catalytic hybridization with multiplex formation to achieve expected advantage of identification of nucleic acid sequence or variation in it. The motivation for this would have been an approach to detect formation of multiple helix structures in hybridization assays.

No claims are Allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 703-308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru.
August 20, 2001

EGGERTON A. CAMPBELL
PRIMARY EXAMINER